Original Article

Clinical and etiopathological profile of pancytopenia in children (1-18 years): A study from tertiary care center of Bundelkhand region, central India

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ABSTRACT

Background: Pancytopenia is defined by a decrease in all three blood components, that is, leukopenia, thrombocytopenia, and anemia below the normal range. This study is an attempt to fill the lacunae regarding the information about pancytopenia in pediatric patients in the Bundelkhand region. The study aimed to study the clinical and etiopathological profile of pancytopenia in children (1–18 years) in the tertiary care center of the Bundelkhand region in central India. **Materials and Methods:** The present study was a hospital-based cross-sectional observational study conducted to learn about the clinical features, demographic and etiopathological profile of pancytopenia in children. The study was performed with 65 patients aged 1–18 years from September 2021 to August 2022 admitted to the Department of Paediatrics, Maharani Laxmi Bai Medical College and Hospital, Jhansi, and fulfilling inclusion criteria. IBM's Statistical Package for the Social Sciences version 23 was used for the statistical study. **Results:** Out of 65 patients, a maximum number of cases were in the age group of 1–6 years (55%). Our study revealed male predominance over females with male-to-female ratio of 2.09:1, mostly belonging to rural areas. The most common presenting complaint was easy fatigue in (90%) of patients followed by fever (54%). The most common physical finding was pallor (100%), followed by splenomegaly and pedal edema (38%) and (18%), respectively. Bone marrow cellularity shows hypocellular marrow (62%), hypercellular (31%), and normocellular (7%). Peripheral smears of most of the patients showed normocytic normochromic (34%), followed by macrocytic hypochromic (30%). Regarding etiology megaloblastic anemia (30%) was reported as the most common cause of pancytopenia followed by malignancies (30%) including myelodysplastic syndrome (9%), multiple myeloma (3%), acute lymphocytic leukemia (9%), and acute myeloid leukemia (9%) followed by aplastic anemia (14%) and sepsis (8%). The study also shows other rare causes of pancytopenia such as disseminated tuberculosis (6%), malaria (9%), and dengue (3%). **Conclusion:** In the present study, the most common etiologies of pancytopenia come out as nutritional causes, that is, megaloblastic anemia followed by malignancies then aplastic anemia.

Key words: Bundelkhand region, Children, Megaloblastic anemia, Pancytopenia

Pancytopenia is diagnosed when the absolute neutrophil count (ANC) is <1.5×10^9/L, the absolute hemoglobin level (Hb) is <10 g%, and the platelet count is <100×10^9/L [1]. The condition is marked as severe, when the patient has Hb <7 g%, ANC <0.5×10^9/L, platelet count 20×10^9/L, and the reticulocyte count is 1% [2]. The frequency of causes of pancytopenia is influenced by demographic factors, therefore in developing countries nutritional and infectious causes prevail whereas in developed countries malignancies manifest as pancytopenia [3]. Studies from various region of India shows varied etiologies of pancytopenia a study from the northern region shows megaloblastic anemia as the most common etiology while in the northeastern region, the study found aplastic anemia as the first most common cause, followed by megaloblastic anemia [4,5]. A study from the western region suggests acute myeloid leukemia (AML) as the most common cause followed by myelodysplastic syndrome and the southern region study shows normoblastic erythroid hyperplasia followed by megaloblastic anemia as causes of pancytopenia [6,7]. To the best of our knowledge, we found no such study from the Bundelkhand region. Hence, it is of paramount importance to know the frequency of causes in the locality for early and effective management of reversible and treatable causes of pancytopenia which further will help in lowering morbidity and mortality, with this background, the present study was conducted to identify the clinical and etiopathological profile of pancytopenia in children admitted at our tertiary care center.

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MATERIALS AND METHODS

The present study was a hospital-based cross-sectional observational study conducted after getting clearance from the institutional ethical committee to study the clinical features, demographic and etiopathological profile of pancytopenia in children at M.L.B. Medical College, Jhansi (U.P.), performed in patients admitted to the Department of Pediatrics from September 2021 to August 2022. With the help of the purposive sampling method, every patient with pancytopenia presenting at our hospital was requested to join our study and undergo bone marrow examination but only 65 patients fulfilling inclusion criteria were recruited in the study after their written and informed consent.

Inclusion Criteria

The following criteria were included in the study:

- Age between 1 and 18 completed years,
- Presenting with signs and symptoms of pancytopenia,
- History of recurrent blood transfusion but not within 1 month,
- Guardian willing to give informed consent.

Exclusion Criteria

Children aged <1 year or more than 18 years, known or previously diagnosed cases of pancytopenia, history of recent blood transfusion, receiving chemotherapy and radiotherapy, known cases of malignancies on chemotherapy/radiotherapy, patients with hemodilution bone marrow aspiration smears, inconclusive bone marrow reports, known case of hemoglobinopathies, history of recent surgery, not willing to give informed consent.

Strategy for Data Collection

On admission, all patients fulfilling inclusion criteria were interviewed for detailed history including the age of presentation, treatment history, family history, history of drug intake, and radiation exposure, and examined for important physical findings such as pallor, icterus, skin pigmentation, the sign of vitamin deficiencies, bone pain, bony tenderness, hepatomegaly, splenomegaly, lymphadenopathy, pedal edema, bleeding manifestation (gum bleed, epistasis, petechial rash purpura, and bleeding from any site), altered sensorium, and ascites. A relevant systemic examination is done to reach the diagnosis. Investigations at the time of admission included a complete hemogram, total and differential leukocyte counts, red blood indices mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration, platelets count, peripheral blood smear, reticulocyte counts, serum iron, serum ferritin, Vitamin B12, folic acids levels, MP smear, typhi dot, blood culture, serology to rule out hepatitis, typhoid, chest X-ray, ultrasonography, a neuroimaging and invasive procedure such as bone marrow examination were done to reach the diagnosis.

Statistical Analysis

IBM's Statistical Package for the Social Sciences version 23 was used for the statistical study (USA). Initially, MS Excel was used to process the data and conduct the coding. Using the Shapiro–Wilk and Kolmogorov-–Smirnov tests, it was determined that the data were not regularly distributed. Frequency and proportions were utilized in the descriptive analysis for categorical variables while mean and standard deviation were employed for continuous variables.

RESULTS

Out of 65 patients aged 1–18 years, a maximum number of cases were in the age group of 1–6 years (55 %), 29% of cases were in the age group of 7–12 years and 16% cases were in the age group of 13–18 years. On a gender basis, 68% were male and 32% were female with male-to-female ratio of 2.09:1. On a geographical basis, 60% of cases were from rural and 40% were from urban areas (Table 1).

The most common presenting complaint was easy fatigue (90%), followed by fever (54%), giddiness (40.0%), palpitation (38.0%), bleeding tendencies (24.0%), lower limb edema (19.0%), cough (18.0%), breathlessness (16.0%), decreased appetite (16.0%), bony pain (14.0%), and loose stool (8.0%). The most common physical finding was pallor (100%), followed by splenomegaly (38%), pedal edema (18%), lymphadenopathy (18.0%), ascites (18.0%), hepatomegaly (18.0%), icterus (14.0%), glossitis (12.0%), knuckle hyperpigmentation (10.0%), and purpuric spots (6.0%) (Table 2).

Bone marrow cellularity shows the majority of patients with hypocellular marrow (62%), followed by hypercellular (31%) and normocellular (7%). A total of 56% of patients had Hb levels between 6.1 and 8 g/dL, while 34% of patients with ≤6 g/dL and 10% of patients between 8.1 and 10 g/dL. Out of the total, 66% of patients presented with a platelet count between 50,000 and 1,50,000 while 34% had a platelet count <50,000. Peripheral smears of most of the patients showed a normocytic normochromic picture (34%), followed by macrocytic normochromic (30%), dimorphic (28%), and normocytic hypochromic (8%) (Table 3).

Table 1: Distribution of study participants based on the demographic profile

Age	No. of cases (n=65)	Percentage
1–6 years	36	55.0
7–12 years	19	29.0
13–18 years	10	16.0
Gender		
Male	44	68.0
Female	21	32.0
Study area		
Rural	39	60.0
Urban	26	40.0

Table 2: Signs and symptoms of study participants

Symptoms	No. of cases (n=65)	Percentage
Easy fatigue	58	90.0
Fever	35	54.0
Giddiness	26	40.0
Palpitation	25	38.0
Bleeding tendencies	15	24.0
Lower limb edema	13	19.0
Cough	12	18.0
Breathlessness	11	16.0
Decreased appetite	11	16.0
Bony pain	9	14.0
Loose stool	6	8.0
Physical findings*		
Pallor	65	100.0
Splenomegaly	25	38.0
Pedal edema	12	18.0
Lymphadenopathy	12	18.0
Ascites	12	18.0
Hepatomegaly	12	18.0
Icterus	9	14.0
Glossitis	8	12.0
Knuckle hyperpigmentation	7	10.0
Purpuric spots	4	6.0

Table 3: Distribution of study participants based on peripheral smear and bone marrow cellularity

Bone marrow cellularity	No. of cases (n=65)	Percentage
Hypo/acellular	40	62.0
Hypercellular	20	31.0
Normocellular	5	7.0
Peripheral smear		
Normocytic normochromic	22	34.0
Macrocytic hypochromic	20	30.0
Dimorphic picture	18	28.0
Normocytic hypochromic	5	8.0

Megaloblastic anemia (30%) came out as the most common cause of pancytopenia, followed by aplastic anemia (14%). Other causes of pancytopenia include myelodysplastic syndrome (9%) acute lymphocytic leukemia (ALL) (9%), AML (9%), and sepsis (8%). The study also revealed other rare causes of pancytopenia such as disseminated tuberculosis (6%), hypersplenism (9%), multiple myeloma (3%), and dengue (3%) (Table 4).

Table 4: Etiological diagnosis of the study population

Etiology	No. of cases (n=65)	Percentage
Aplastic anemia	9	14.0
Acute leukemia	6	9.0
Acute myeloid leukemia	6	9.0
Disseminated tuberculosis	4	6.0
Hypersplenism	4	6.0
Megaloblastic anemia	19	30.0
Malaria	2	3.0
Myelodysplastic syndrome	6	9.0
Multiple myeloma	2	3.0
Sepsis	5	8.0
Dengue	2	3.0

DISCUSSION

Pancytopenia is a common feature of many diseases. In our study, out of 65 children with pancytopenia, the majority (55.0%) were of the age group 1–6 years, followed by 7–12 years of age (29.0%) showing that the prevalence of pancytopenia in this study was highest among 1–6 years age group patients. This finding is similar to studies by Singh *et al*. [8] and Gupta *et al*. [9], where the majority of patients were between 1 and 5 years of age group, that is, 51.6% and 58%. Rathod *et al*. [10] showed a majority of patients between 6 months and 5 years of age group (39%). However, Chouthai and Kulkarni [11] showed a majority of patients between the 10 and 12 years of age group (31%) presenting as pancytopenia followed by the 7–9 years of age group (24%) and 13–15 years of age group (23%). The explanation for this difference may be due to different geographical and sociocultural practices. The present study shows male preponderance over female with a ratio of 2.09:1, various studies showed similar observation, that is, Gayathri and Rao [4], 1.2:1. Santra and Das 1.47:1 [12], Reddy and Rao *et al*. [13], 1.2:1 and Khunger *et al*. [14], 1.2:1. This outcome is in contrast to the study conducted by Pathak *et al*. [15], where male-to-female ratio was 1:1.04. In the present study, the most common presenting symptoms in children with pancytopenia were easy fatigue (90%) and fever (54%), followed by giddiness (40%) and palpitations (38%). Gayathri *et al*. [4] also showed generalized weakness 100% as the most common presenting symptom. Deshpande *et al*. [16] showed generalized weakness at 46.7% as the first most common symptom followed by fever at 24.2%. While study by Santra and Das. [12] showed fever as the most common presenting symptom 50.45%, followed by weakness 45.04%, bleeding manifestation 41.44%, and breathlessness 32.43%.

In the present study, pallor was present in all children (100%), followed by splenomegaly (38%), pedal edema (18%), and lymphadenopathy (18%), which is similar to the study done by Deshpande *et al*. [16], in which all children with pancytopenia had pallor (100%), followed by icterus 24.16%, splenomegaly 15%, and hepatomegaly 11.6%. In our study, the nutritional cause came out to be the most frequent etiology of pancytopenia, that is, megaloblastic anemia that was discovered to be 30% (19 out of 65 participants studied). This was followed by aplastic anemia, myelodysplastic syndrome, ALL, AML, and sepsis. A similar finding was observed in a study conducted by Gayathri *et al*. [4], which reported megaloblastic anemia (74.04%) as the most common cause followed by aplastic anemia (18.26%). A study by Deshpande *et al*. [16] found megaloblastic anemia (72%) as the first-most common cause followed by aplastic anemia (14%). Similar results were reported by Reddy and Rao [13] and

Deshpande *et al*. [16], that is, megaloblastic anemia was found in 38.1% and 72.6% of cases. In contrast to our study, a study done by Santra *et al*. [12] found aplastic anemia as the most common cause (22.72%).

CONCLUSION

Demographic factors may affect the frequency of causes of pancytopenia in different populations. Knowing the cause of pancytopenia in a particular geographical area may add to early diagnosis and evaluation. The present study finds nutritional deficiency, that is, megaloblastic anemia as the most common cause of pancytopenia from the Bundelkhand region in children mostly belonging to rural areas. As the nutritional cause is treatable and preventable so this study suggests the need for necessary action to improve the nutritional status of children and adolescents in this region in the form of fortification of food, Vitamin B12, and folic acid supplementation. Early diagnosis and effective treatment of reversible causes further lead to the lowering of morbidity and mortality.

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